

A

Mendel Lecture

Molecular Genetics: the present position

Honoured

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Two aspects of molecular genetics -
from the genetic side

do genetic experiments which need a fairly detailed
knowledge of molecular basis to interpret correctly.

(example: genetic determinants of antigenic complementation)

from the molecular biology side

aim to explain biology (e.g. fundamental processes)
in molecular terms.

This is needed as a tool.

example: co-linearity of gene + protein ————— S
why tool is needed:

① DNA is difficult to study (base sequence etc)
by biochemistry

② in vitro synthesis is often unreliable; &
also all is complex.

note on the other hand that gene expression now
always been studied in plant cells: may be better to
grow cells and see our the "gen product": protein.

B

Mendel Lecture

Molecular Genetics: The present position

Horizontal

Difficultly about title.

Too broad. Thus will omit

- ① recombination : breakage repair, not copy choice
repair mechanisms.

can recombine between adjacent bases. — S

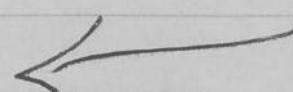
- ② control mechanism : it can involve groups of genes
(ie of rate of gene action) group is polar (operator)
also polar mutants exist
(reversed type of mutation)

but inhibitor is complicated, especially as

- ③ not sure if protein synthesis involved in rRNA production.
④ little known about rRNA destruction.

What are the basic problems of molecular genetics?

- ① What are genes made of?
- ② How are they joined together? chromosome structure.
- ③ How are genes copied? and how do mutations occur
- ④ What are mutations? and how are they produced?
- ⑤ How do genes act? ie what is am the gene products.
- ⑥ What controls the rate of action?
- ⑦ What is mechanism of genetic recombination



C

Second Perturbation

to micro-organisms.

partly because most of our knowledge comes from micro-organisms.

- advantages because
- ① large populations + selective techniques.
 - ② rapid growth - growth experiments
 - ③ growth requirements simple.

Also because they are actually simpler
"chromosome" is simpler.

more like "enzymes in a bag" than higher cells.
i.e. less ultrastructural spatial interaction.

but side-references to higher organisms

Plan of Lecture

General Survey : in broad terms.

Then critical comments.

Y

Mendel Lecture

Title too wide : full coverage impossible.

Thus limit - recombination and ^(mainly) control also replication

also mainly apply to microorganisms

but not the spread mechanism of microorganisms.

Plan

General survey first & to give portion in outline

Then critical evaluation.

Importance of microorganisms :

① large populations + selective techniques
makes for fine genetic mapping

② rapid growth makes experiments quick

③ "defined medium" helps in planning
experiments

[④ fairly easy to get at their proteins.]

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General Survey

DNA \rightarrow mRNA \rightarrow protein
+ rRNA \rightarrow protein.

Genetic material is nuclear acid.

usually DNA, but RNA is some viruses.

usually double-stranded, but occasionally single-stranded for some small viruses.
length very long compared with single genes.

Replication of Genetic material

is by ^{standard} base-pairing mechanism. ~~If~~ Normally
semi-conservative (define). for single-stranded, simpler
a double-stranded replication intermediate
ie a rather direct, simple mechanism.

Expression of Genetic material

by making an RNA ~~as~~ copy of one strand
(unnecessary for single-stranded RNA viruses)
and usually this RNA used as a messenger for
protein synthesis. Then main function of
genes is to control the sequence of proteins.

Protein synthesis

involves complicated biochemical machinery.
 (e.g. ribosomes, activating enzymes, tRNA etc.)

translate by means of a non-overlapping, ~~one~~ triplet code, most triplets starting for amino acids. probably universal.

Affinity

Protein folding

common to fold up itself (by and large)
 3-D structure gives the specificity etc for enzyme action
 or for use a structural components.

many proteins are aggregates of identical subunits.

[allostery : idea that an unrelated small molecule can influence its conformation and thus the rate of a enzyme action]

Catalytic mechanisms poorly understood.
 clear that for rate of gene action can be controlled
 by small protein molecules, not by means of c. motor.
 these genes are often interested in groups.
 prob polar effects

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General remarks

Molecular biology
Lectures by J.
Sohar (in notes)

② character of NA and protein

NA - very limited function, but ideal
for replication

protein - very versatile, but ~~not~~ no
easy replication mechanism.

③ Bauz plan

1D genetic information }
→ 1D amino acid sequence }
→ 3D protein structure.

④ Nature of genetic material

— not inertial state
— not plastic.

Detailed Enunciation

① NA is the genetic material

(a) nor crystal-clear what genetic material means.

prob. means material most simply replicated.

or contains all (most) information needed to make cell
^{alive}
 need to borrow ^{some} information, which is then paid back.

but must be self-consistent.

② cytoplasmic factors : probably due to special DNA

e.g. mitochondria and chloroplasts.

shown to exist, but "whether known about what they do

③ other factors e.g. nucleolar factors

probably exist. not clear how stable they

as alternative would be ; nor how many
 of them.

(d) in all NA "Genetic" ⁽ⁱ⁾ is it all copied.

no. no evidence that RNA is copied in most

normal cells (but is in virus-infected cells)
medical implication

(ii) does all DNA code for protein
or, some clearly code for rRNA and tRNA
may be other examples.

however regulatory genes don't produce protein
(may be nucleoprotein)

but all DNA?

e.g. DNA of e.g. amphibia & newts
of each species AT DNA.

important because would like to estimate
the number of genes. also other factors
will be important.

?

② Nature of the "chromosome"

E. coli: one long piece NA, often circular

Sometimes circularly permuted

E. coli: one very long piece DNA, in form
of a circle.

Higher organisms

obscure: probably several circles
probably several per chromosome.

arrangement unclear.

role of proteins (histones) still

obscure

Mc Dermott.

DNA replication

Evidence for semi-conservation fairly good

also in special cases one chain come apart.

but no ^{increase} replication of a single DNA in test-tube by helicase enzyme.

also problem of direction of replication?
?

is it C repair enzyme?

if so, what is the true enzyme like?

is it generally located in the cell.

conclusion problem still very unsatisfactory.

RNA RNA replication

only one case in which evidence of

biological activity, then mechanism controversial.

also described action of enzyme ie base pairing, not yet established.

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making RNA from DNA

- reasonable evidence there only one chain is copied.

but don't know signal for start
- - - - stop

[only rather vague idea about control of rate]

don't really know if perhaps ribosomes
(i.e. protein synthesis) play a role in mRNA reading.

don't know details of mechanism ie is there a
running loop? or is double helix never unzipped.

but evidence does suggest complementary synthesis
(because will work on single strand)

so far no simple mutants [ie an opposed to
deletion] which appear to give start or stop signals.]

Motai system

Genetic code

- ~~the~~ punctuation marks need further study
- What are minor tRNA's for?
- Is there ambiguity?
- Is there modulation (appear from punctuation mark effect.)?
- Is it really universal?

Structure of code - - possible

(origin of code?)

Introducing
~~not~~ Suppose a error in
 protein synthesis.

General conclusion

We see that ~~for most of the~~ ^{this} problems of molecular genetics fall into two classes,

- ① Gene structure
 - Gene replication
 - Gene action
 - Nature of mutation
- } all solved
 in outline
-
- ② gene control
 - reproduction
- } look at these they
 may be solved soon.

Future development

- to extend to larger structures and higher organisms
 eg. Chromosome structure
 "Structure and " " "
 to study biological chemistry in more detail
 eg. replication process; base pairing.